

## WHAT IS CLAIMED IS:

1. A fusion protein having an amino acid sequence from the ART protein fused at its carboxy terminus to one or more amino acid sequences not derived from the ART protein, where the amino acid sequence from the ART protein is selected from the group consisting of: SEQ.ID.NOs.:6-8 and 9.
2. The fusion protein of claim 1 having an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-5, 10-19, and 20.
3. The fusion protein of claim 2 having the amino acid sequence of SEQ.ID.NO.:2.
4. An ART polypeptide having an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:6-8 and 9.
5. A DNA sequence encoding the fusion protein of claim 1.
6. A method of determining whether a substance is an inhibitor of the binding of an ART polypeptide to a melanocortin receptor where the method comprises:
  - (a) providing cells expressing the melanocortin receptor;
  - (b) exposing the cells to a chosen concentration of the melanocyte stimulating hormone in the absence of the ART polypeptide and in the absence of the substance and measuring the amount of melanocyte stimulating hormone binding to the cells to obtain a first value for melanocyte stimulating hormone binding;
  - (c) exposing the cells to the chosen concentration of melanocyte stimulating hormone in the presence of a chosen concentration of the ART polypeptide and in the absence of the substance and measuring the amount of melanocyte stimulating hormone binding to obtain a second value for melanocyte stimulating hormone binding where the second value for melanocyte stimulating hormone binding indicates that less melanocyte stimulating hormone binding has occurred as compared to the first value for melanocyte stimulating hormone binding;

(d) exposing the cells to the chosen concentration of melanocyte stimulating hormone in the presence of the chosen concentration of ART polypeptide and in the presence of the substance and measuring the amount of melanocyte stimulating hormone binding to obtain a third value for melanocyte stimulating hormone binding;

where, if the third value for melanocyte stimulating hormone binding is greater than the second value, then the substance is an inhibitor of the binding of the ART polypeptide to the melanocortin receptor;

where the ART polypeptide has an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-19 and 20.

7. The method of claim 6 where the melanocortin receptor is selected from the group consisting of: the melanocortin-3 receptor (MC3R) and the melanocortin-4 receptor (MC4R).

8. A method for determining whether a substance is an inhibitor of the binding of an ART polypeptide to a melanocortin receptor where the method comprises:

- (a) providing cells expressing a melanocortin receptor;
- (b) exposing the cells to an ART polypeptide in the presence and in the absence of the substance under conditions such that if the substance were not present, the ART polypeptide would bind to the melanocortin receptor;
- (c) measuring the amount of binding of the ART polypeptide to the melanocortin receptor in the presence and in the absence of the substance;

where a decrease in the amount of binding of the ART polypeptide to the melanocortin receptor in the presence as compared to the absence of the substance indicates that the substance is an inhibitor of the binding of the ART polypeptide to the melanocortin receptor;

where the ART polypeptide has an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-19 and 20.

9. The method of claim 8 where the melanocortin receptor is selected from the group consisting of: the melanocortin-3 receptor (MC3R) and the melanocortin-4 receptor (MC4R).

10. A method for determining whether a substance is an allosteric enhancer of the binding of an ART polypeptide to a melanocortin receptor where the method comprises:

- 5 (a) providing cells expressing a melanocortin receptor;  
(b) exposing the cells to an ART polypeptide in the presence and in the absence of the substance under conditions such that if the substance were not present, the ART polypeptide would bind to the melanocortin receptor;  
(c) measuring the amount of binding of the ART polypeptide to the  
10 melanocortin receptor in the presence and in the absence of the substance;  
where an increase in the amount of binding of the ART polypeptide to the melanocortin receptor in the presence as compared to the absence of the substance indicates that the substance is an allosteric enhancer of the binding of the ART polypeptide to the melanocortin receptor;  
15 where the ART polypeptide has an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-19 and 20.

11. The method of claim 10 where the melanocortin receptor is selected from the group consisting of: the melanocortin-3 receptor (MC3R) and the  
20 melanocortin-4 receptor (MC4R).

12. A method for determining whether a substance is a functional inhibitor of the antagonistic effect of an ART polypeptide on a melanocortin receptor where the method comprises:

- 25 (a) providing cells expressing a melanocortin receptor;  
(b) exposing the cells to a melanocyte stimulating hormone selected from the group consisting of:  $\alpha$ -melanocyte stimulating hormone,  $\beta$ -melanocyte stimulating hormone, and  $\gamma$ -melanocyte stimulating hormone, in order to activate the melanocortin receptor, leading to the production of cAMP;  
30 (c) exposing the cells to an ART polypeptide in the presence and in the absence of the substance under conditions such that if the substance were not present, the ART polypeptide would inhibit the production of cAMP mediated by the melanocortin receptor;

(d) measuring the amount of cAMP produced the presence and in the absence of the substance;

where an increase in the amount of cAMP produced in the presence as compared to the absence of the substance indicates that the substance is a functional inhibitor of the antagonistic effect of the ART polypeptide on the melanocortin receptor;

where the ART polypeptide has an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-19 and 20.

10 13. The method of claim 12 where the melanocortin receptor is selected from the group consisting of: the melanocortin-3 receptor (MC3R) and the melanocortin-4 receptor (MC4R).

15 14. A method of determining whether a substance is an inhibitor of the effect of an ART polypeptide comprising:

(a) providing a *Xenopus* melanophore cell line;

(b) exposing the *Xenopus* melanophore cell line to a chosen concentration of  $\alpha$ -melanocyte stimulating hormone in the absence of the ART polypeptide and in the absence of the substance and measuring the amount of pigment dispersion to obtain a first value for pigment dispersion;

20 (c) exposing the *Xenopus* melanophore cell line to the chosen concentration of  $\alpha$ -melanocyte stimulating hormone in the presence of the ART polypeptide and in the absence of the substance and measuring the amount of pigment dispersion to obtain a second value for pigment dispersion where the second value for pigment dispersion indicates that less pigment has been dispersed as compared to the first value for pigment dispersion;

25 (d) exposing the *Xenopus* melanophore cell line to the chosen concentration of  $\alpha$ -melanocyte stimulating hormone in the presence of the ART polypeptide and in the presence of the substance and measuring the amount of pigment dispersion to obtain a third value for pigment dispersion;

30 where if the third value for pigment dispersion indicates that more pigment has been dispersed as compared with the second value, then the substance is an inhibitor of the effect of the ART polypeptide;

where the ART polypeptide has an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-19 and 20.

- 5           15.     A method of determining whether a substance is an inhibitor of the binding of an ART polypeptide to a melanocortin receptor comprising:
- (a)     providing cells expressing the melanocortin receptor;
  - (b)     exposing the cells to a chosen concentration of the melanocyte stimulating hormone and a chosen concentration of the ART polypeptide in the presence and in the absence of the substance and measuring the amount of melanocyte stimulating hormone binding to the cells in the presence and in the absence of the substance;
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              where an increase in the amount of melanocyte stimulating hormone binding in the presence of the substance indicates that the substance is an inhibitor of the binding of an ART polypeptide to a melanocortin receptor;

- 15                 where the ART polypeptide has an amino acid sequence selected from the group consisting of: SEQ.ID.NOs.:1-19 and 20.

16.     The method of claim 15 where the melanocortin receptor is selected from the group consisting of: the melanocortin-3 receptor (MC3R) and the melanocortin-4 receptor (MC4R).
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